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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,167	08/15/2000	Bernard Knoops	VANM143.001A	2578

20995 7590 06/18/2002

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 06/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,167	KNOOPS ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed *after* SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9 and 12-27* is/are pending in the application.

4a) Of the above claim(s) *13,15 and 17-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,9,12,14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 5, 9 and 12-27 are pending.

2. Claims 13, 15 and 17-27 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. In view of the amendment filed 2/11/02, the following rejections remain.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. The request to insert the attached abstract in the amendment filed 2/11/02, is acknowledged. However, the attached abstract was not found.

5. The disclosure stands objected to because of the following informalities: (1) SEQ ID NO: is required on page 18, line30; (2) the "n°" on page 20 lines 23-27 should have been "No.".

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 5, 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) two human polynucleotides consisting of SEQ ID NO: 1 and 10, a rat polynucleotide of SEQ ID NO: 3 and a mouse polynucleotide of SEQ ID NO: 5 that encode a peroxisomal-associated polypeptides corresponding to SEQ ID NOS: 2, 4 and 6, respectively, and polynucleotide probes of SEQ ID NOS: 7-9, and 11-16 (See page 7 of the specification) for in vitro diagnosis, **does not** reasonably provide enablement for (1) *any* "pharmaceutical composition" comprising a pharmaceutical acceptable carrier and *any* polynucleotide mentioned above or its complementary strand and a cell transformed by *any* vector comprising (1) *any* partial or total "genomic deletion" of SEQ ID NO: 1 or (3) *any* "homolog thereof". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only (1) a human polynucleotide (cDNA) consisting of SEQ ID NO: 1 and 10, a rat polynucleotide of SEQ ID NO: 3 and a mouse polynucleotide of SEQ ID NO: 5 encoding a peroxisomal-associated polypeptides corresponding to SEQ ID NOS: 2, 4 and 6, from human, rat and mouse, respectively, (2) polynucleotide probes of SEQ ID NOS: 7-9 for in vitro diagnosis or monitoring lung injury associated with oxidative stress-related disorder.

The specification does not provide any guidance as how to use *any* polynucleotide mentioned above for a pharmaceutical composition for treating *any* disease. Further, there are no *in vivo* working examples to demonstrate that any gene therapy using said composition would be effective in treating any disease. A "pharmaceutical composition" comprises a "polynucleotide sequence encoding a peptide for treating any diseases in the absence of *in vivo* data is unpredictable for the following reasons: (1) efficacy of the polynucleotide has not been definitively demonstrated; (2) it is not always possible to extrapolate directly from in vitro experiments to in vivo studies; (3) the enhancing or maintaining high level expression of genes transferred to somatic cells may not persist or consistently achieved; (4) appropriate expression of polynucleotide transfer to specific cell types (target specificity) has not been demonstrated; (5) adverse reactions from the recipient may result; (6) the lower efficiency of gene transfer (naked nucleic acid) compared with viruses and the effective therapeutic amount have not been addressed.

Das *et al* (of record) teach that getting the antisense to the cell nuclei where their anti-gene action can take place can be difficult (See abstract, in particular).

Verma *et al* (of record) teach that the problem of gene therapy is the inability to deliver genes efficiently to the right type of cell, obtaining sustained expression of the therapeutic protein and without triggering the host immune responses (See page 239, in particular). Therefore, in the

absence of in vivo working examples, it would require undue experimentation of one skilled in the art to practice the claimed invention.

In re Fisher, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention without undue amount of experimentation. As such, further research would be required to practice the claimed invention.

Applicants' arguments filed 2/11/02 have been fully considered but are not found persuasive.

Applicants' position is that the claims have been amended to recite an isolated or purified polynucleotide comprising SEQ ID NO: 1 or its complementary strand.

However, claim 16 still recites a partial or total genomic deletion of SEQ ID NO: 1 or a homolog thereof" while claim 14 still recites a pharmaceutical composition.

8. Claims 5, 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** for a cell transformed by *any* vector comprising (1) *any* partial or total "genomic deletion" of SEQ ID NO: 1 or (2) *any* homolog thereof", and (3) *any* "pharmaceutical composition for treating any disease.

The specification as filed discloses only (1) two human polynucleotide consisting of SEQ ID NO: 1 and 10, a rat polynucleotide of SEQ ID NO: 3 and a mouse polynucleotide of SEQ ID NO: 5 that encode a peroxisomal-associated polypeptides of SEQ ID NOS: 2, 4 and 6 and polynucleotide probes of SEQ ID NOS: 7-9, and 11-16 (See page 7 of the specification).

There is a lack of a written description about the structure associated with function of *any* "partial or total genomic deletion" of SEQ ID NO: 1 *or any* "homolog thereof" for in vitro diagnosis or for in vivo treatment of any disease. Given the lack of a written description of *any* additional representative species of polynucleotide as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *see University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 2/11/02 have been fully considered but are not found persuasive.

Applicants' position is that the claims have been amended to recite an isolated or purified polynucleotide comprising SEQ ID NO: 1 or its complementary strand.

However, the claim 14 still recites a pharmaceutical composition while claim 16 still recites "a partial or total genomic deletion of SEQ ID NO: 1 or a homolog thereof" while claim 14 still recites a pharmaceutical composition.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 5, 9, 12, 14 and 16 stand rejected under 35 U.S.C. 102(e) as being anticipated by the US Pat No. 6,197,543 (Filed Oct 1997, PTO 892).

The '543 patent teaches an isolated or purified polynucleotide (See reference SEQ ID NO: 2 of '543 patent, in particular) that is 99.1% identical to the claimed polynucleotide of SEQ ID NO: 1 and its complementary strand. The reference polynucleotide encodes an amino acid sequence 100% identical to the polypeptide of SEQ ID NO: 2 of instant application (See polynucleotides 193 to 990 of reference polynucleotide SEQ ID NO: 2 of the '543 patent, in particular). The transitional phrase "comprising" is open-ended and it opens up the polynucleotide to include additional nucleotide at either or both ends. Therefore, the claim reads on the reference polynucleotide. The '543 patent teaches partial nucleotide sequence or primers comprising more than 15 base pairs or a portion of the reference SEQ ID NO: 2 of the '543 patent (See column 15, lines 57-66 bridging column 16, lines 1-11, in particular). The '543 patent further teaches a vector and host cell transformed with the reference polynucleotide or a fragment

thereof to express the polypeptide (see column 17, lines 53- 67 bridging column 18, lines 1-2, column 20, lines 64-67 bridging column 21, lines 1-8, column 41, Expression of VMP, in particular). The '543 patent also teaches a diagnostic device such as microarray comprising the reference polynucleotide or a portion thereof as a target to monitor the expression level of large number of genes simultaneously (See column 33, lines 17-51, in particular). The '543 patent further teaches a pharmaceutical composition comprising a pharmaceutically acceptable carrier and the reference nucleotide sequence of SEQ ID NO: 2. Since the reference polynucleotide is 99.1% identical to SEQ ID NO: 1 of instant application, the reference polynucleotide anticipates the claimed 70%, 85% and 95% homologous to SEQ ID: NO: 1 or its complementary strand. Given that the reference polynucleotide encodes an amino acid sequence that is 100% identical to the polypeptide of SEQ ID NO: 2 of instant application, the reference polypeptide anticipates the claimed polynucleotide encoding an amino acid sequence more than 70% homologous to SEQ ID NO: 2 of instant application. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 2/11/02 have been fully considered but are not found persuasive.

Applicants' position is that the claims have been amended to recite an isolated or purified polynucleotide comprising SEQ ID NO: 1 or its complementary strand.

However, the phrase "comprising" is open-ended. It expands the claimed polynucleotide to include additional nucleotides at either or both ends. Further, claim 16 still recites a "homolog thereof".

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 9 and 16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al (Accession No. W00593, April 1996, PTO 892) or Hillier et al (Accession No. N91311, April 1996, PTO 892), or Hillier et al (Accession No. W38597, May 1996, PTO 892), or Hillier et al (Accession No. N68467, March 1996, PTO 892), or Hillier et al (Accession No. N42215, Jan 1996, PTO 892), or Hillier et al (Accession No. H20154, July 1995, PTO 892) or Marra et al (Accession No. W71344, June 1996, PTO 892), each in view of Sambrook et al (*Molecular Cloning*, 1989, Cold Spring Harbor Laboratory, CSH, NY, Ch. 17).

The teachings of Hillier et al have been discussed supra.

The claimed invention in claim 9 differs from the references only by the recitation of a vector comprising the said polynucleotide.

The claimed invention in claim 16 differs from the references only by the recitation of a cell transformed by the vector comprising a partial or genomic deletion of polynucleotide of SEQ ID NO: 1 or a homologue thereof.

Marra *et al* teach a partial polynucleotide from the mouse which is a homolog of a partial polynucleotide of SEQ ID NO: 1 of instant application.

Sambrook *et al* teach cloning a cDNA into an expression vector, and a process of transforming the expression vector into host cells, culturing the host cells under conditions in which the polypeptide is expressed and then recovering the polypeptide from the culture. Sambrook *et al* teach that it is desirable to use recombinant DNA techniques for the production of biologically active proteins in order to produce proteins of higher concentration and purity.

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce a peptide of interest using a portion of polynucleotide that is specific for SEQ ID NO: 1 of instant application as taught by Hillier et al or a portion of a polynucleotide from a homolog such as a mouse as taught by Marra et al by constructing an expression vector using the reference polynucleotide portion thereof to produce a recombinant host cell using the said expression vector and culturing the host cell under conditions which express the polypeptide in order to recover the polypeptide from the culture as taught by the Sambrook et al.

One having ordinary skill in the art at the time the invention was made would have been motivated to produce the polypeptide using recombinant techniques because there would be a higher yield of polypeptide with greater purity as taught by Sambrook *et al.*

Applicants' arguments filed 2/11/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claimed invention recites a vector comprising SEQ ID NO: 1 or its complementary strand and a cell transformed by the vector or comprising a partial or total genomic deletion of SEQ ID NO: 1 or a homolog thereof and (2) recent research has shown the significant of SEQ ID NO: 1 as a potential tool in diagnostic and therapeutic applications, an example such as single nucleotide polymorphisms (SNPS) of Homosapiens peroxiredoxin 5 gene (PRDX5) have been report in the public databases. Some of these SNPS are in the coding region of the gene. PRDX5 SNPs are relevant to the identification of susceptibility to lung injuries and diseases and oxidative stress disorder since recombinant PRDX5 protein is shown to provide protection against excitotoxic insults in the central nervous system. Free radical production participates in the formation of NMDA receptor-mediated brain lesions.

However, the argument of counsel is irrelevant to this rejection.

14. No claim is allowed.

15. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be

left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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June 17, 2002

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